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OMB APPROVAL NUMBER: 0693-0009

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U.S. DEPARTMENT OF
NATIONAL INSTITUTE OF STANDARDS AND TE

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SINGLE COMPANY AI O (ATP) PR

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2001-3I

Public reporting burden for this collection (response, including the time for reviewing instructions, searching existing data sources, gathering and maintai collection of information. Send comments regarding this burden estimate or any other aspect of this collectio burden, to Director, Advanced Technology Program, National Institute of Standards and Technology, 100 Bureau Drive, Stop 4700, Administration Building, Room A333, Gaithersburg, Maryland 20899-4700.

1. COMPETITION NUMBER: Competition 00-01

2. TECHNOLOGY AREA CODE: B0600 / I0400

3. PROJECT DURATION: 3 (Three) YEARS 36 MONTHS

4.A. OTHER ATP SUBMISSIONS — LIST PROPOSAL NUMBER(S) OF SUBSTANTIALLY OVERLAPPING PROPOSAL(S) PREVIOUSLY SUBMITTED: NONE

4.B. IF SUBMITTING A CONCURRENT SUBSTANTIALLY OVERLAPPING PROPOSAL TO ANOTHER CURRENT OR PENDING ATP COMPETITION, LIST COMPETITION NUMBER(S): NONE

5. LEGAL NAME, ADDRESS, AND WEBSITE OF SUBMITTING ORGANIZATION

Computer Aided Surgery, Inc.
300 East 33rd Street
Suite 4N
New York, New York 10016

http://www.casi.net

6. TYPE OF ORGANIZATION (CHECK ALL THAT APPLY)

- [X] PROFIT - SMALL BUSINESS
- [ ] PROFIT - LARGE BUSINESS
- [ ] PROFIT - MEDIUM BUSINESS
- [ ] FOREIGN-OWNED U.S. SUBSIDIARY

7. EMPLOYER IDENTIFICATION NUMBER (EIN): E.I.N. #13-388-9180

8. DUN AND BRADSTREET NUMBER: D-U-N-S 94-285-4266

9. NAME OF PRINCIPAL INVESTIGATOR AT SUBMITTING ORGANIZATION (Address required, if different than item 5)

Dr.D. B. Karron (Ph.D.)
Chief Technical Officer
Computer Aided Surgery, Inc.

TELEPHONE NUMBER: +1 (212) 686 8748
FAX NUMBER: +1 (212) 448 0261
E-MAIL ADDRESS: karron@casi.net

10. NAME OF GRANT/CONTRACT MANAGER AT SUBMITTING ORGANIZATION (Address required, if different than item 5)

Dr. D. B. Karron
President
Computer Aided Surgery, Inc.

TELEPHONE NUMBER: +1 (212) 686 8748
FAX NUMBER: +1 (212) 448 0261
E-MAIL ADDRESS: karron@casi.net

11. SOURCES OF FUNDS	YEAR ONE	YEAR TWO	YEAR THREE	TOTAL
A. ATP (DIRECT COSTS ONLY)	$ 800,000	$ 600,000	$ 600,000	$ 2,000,000
B. PROPOSER	$ 30,000	$ 30,000	$ 40,000	$ 100,000
C. TOTAL (A + B)	$ 830,000	$ 630,000	$ 640,000	$ 2,100,000

12. PROPOSAL TITLE

Anatomic Computer Modeling for Precise and Accurate Therapies

13. NON-PROPRIETARY PROPOSAL ABSTRACT

Computer Aided Surgery, Inc. will develop a new computer application server that will take calibrated, encrypted raw images from a clients' medical imaging instrumentation (MRI, CT, Ultrasound, etc.), over the internet.
Our system will rapidly generate encrypted, precise, accurate, and variable resolution three dimensional tiled models applicable for diverse applications as radiation therapy, surgical planning, intraoperative guidance, rapid manufacturing of prosthesis, verification of surgical results, robotic surgery trajectory planning, patient communication, education and other customer specific applications
The novel idea, that enables the technological leap forward is Digital Morse Theory.
The essential insight of Digital Morse Theory is that it describes the behaviour of three dimensional SpiderWeb surfaces surfaces in terms of Morse Critical features.
These surfaces are the computational building tiles of the biologically and medically important objects we wish to parse from an opaque brick of bytes that compromise a volume data set.
We can build an index of all of the objects in a volume to utilize these elements in terms of their generator critical points. Our novel geometric construction algorithms will be embodied in a network -sed application service provider model. The server will upload from the radiological diagnostic image -ducer, and download to the therapeutic consumer model. We will function as a unique, super specialty medical imaging Internet Service Provider.

GOVERNMENT EXHIBIT 10
07 Cr. 541 (RPP) (ID)

ADMINISTRATION/PSG ELECTRONIC FORM

EXCEPTION TO STANDARD FORMS 424 AND 424A APPROVED BY GSA 4-91

14. CERTIFICATION: BY SIGNING THIS PROPOSAL COVER SHEET, I CERTIFY, TO THE BEST OF MY KNOWLEDGE AND BELIEF, THAT ALL INFORMATION IN THIS PROPOSAL IS TRUE AND CORRECT AND THAT:

A. THIS PROPOSAL IS NOT REQUESTING FUNDING FOR EXISTING OR PLANNED RESEARCH PROGRAMS THAT WOULD BE CONDUCTED IN THE SAME TIME PERIOD IN THE ABSENCE OF FINANCIAL ASSISTANCE UNDER THE ATP.

B. ALL INDIRECT COSTS PROPOSED IN THIS PROPOSAL ARE INCLUDED UNDER THE PROPOSER'S COST SHARE AND NO INDIRECT COSTS ARE INCLUDED IN THE ATP SHARE OF COSTS REQUESTED.

C. IF A LARGE BUSINESS, COST SHARING PROPOSED BY THE LARGE BUSINESS IS AT LEAST 60 PERCENT OF EACH YEAR'S TOTAL COSTS.

D. THE TOTAL VALUE OF ANY IN-KIND CONTRIBUTIONS DOES NOT EXCEED 30 PERCENT OF THE COMPANY'S TOTAL COST SHARE.

E. THE FOLLOWING QUESTIONS HAVE BEEN TRUTHFULLY ANSWERED:

		YES	NO
i.	IS THE COMPANY DELINQUENT ON ANY FEDERAL DEBT? (IF YES, EXPLAIN IN ITEM 15, REMARKS.)	☐	☒
ii.	WAS PROPOSAL OR VERY SIMILAR PROPOSAL SUBMITTED TO ANOTHER FEDERAL AGENCY? (IF YES, EXPLAIN IN ITEM 15, REMARKS.)	☐	☒
iii.	DOES THE COMPANY HAVE A PARENT COMPANY OUTSIDE THE UNITED STATES? (IF YES, IDENTIFY THE PARENT COMPANY AND ITS PLACE OF INCORPORATION IN ITEM 15, REMARKS.)	☐	☒
iv.	IS THE COMPANY MAJORITY OWNED BY INDIVIDUALS WHO ARE NOT CITIZENS OF THE UNITED STATES? (IF YES, EXPLAIN IN ITEM 15, REMARKS.)	☐	☒
v.	IS THE COMPANY SUBJECT TO CONTROL BY INDIVIDUALS WHO ARE NOT CITIZENS OF THE UNITED STATES? (IF YES, EXPLAIN IN ITEM 15, REMARKS.)	☐	☒
vi.	DOES THE PROPOSED R&D INVOLVE THE USE OF HUMAN SUBJECTS AND/OR HUMAN TISSUE, AND/OR HUMAN CELL LINES? (IF YES, EXPLAIN IN ITEM 15, REMARKS, AND INDICATE WHETHER OR NOT THE RESEARCH PLAN HAS BEEN REVIEWED AND APPROVED BY AN INSTITUTIONAL REVIEW BOARD (IRB).)	☐	☒
vii.	DOES THE PROPOSED R&D INVOLVE THE USE OF VERTEBRATE ANIMALS? (IF YES, EXPLAIN IN ITEM 15, REMARKS, AND INDICATE WHETHER OR NOT THE RESEARCH PLAN HAS BEEN REVIEWED AND APPROVED BY AN ANIMAL CARE AND USE COMMITTEE.)	☐	☒

15. REMARKS (CONTINUE ON A SEPARATE SHEET IF NECESSARY)

16. DESCRIBE WHAT EFFORTS WERE MADE, PRIOR TO APPLYING FOR ATP FUNDING, TO SECURE PRIVATE CAPITAL TO SUPPORT THIS PROJECT WHOLLY.

CASI's reputation as a basic research company has made our efforts to raise private capital for this high risk project difficult
Traditional paths to commercalization financing would require many years of academic research,
which private equity will not fund.

Our goal is to use ATP funding to go directly from preliminary results with a novel proven theory to market dominance
intellectual property available to all medical and scientific customers over the internet.

17. AUTHORIZED COMPANY REPRESENTATIVE (TYPE NAME AND TITLE)

B. Karron, PhD President and CTO, Computer Aided Surgery, Inc.

18. TELEPHONE NUMBER

+1 (212) 686 8748

SIGNATURE

D B Karron PhD

D. B. Karron, PH.D. President and C.T.O.

20. DATE

July 6, 2001

ESTIMATED MULTI-YEAR BUDGET - SINGLE COMPANY				
	YEAR ONE	YEAR TWO	YEAR THREE	TOTAL
1. OBJECT CLASS CATEGORY				
A. Personnel Salaries / Wages	$375,000	$375,000	$375,000	$1,125,000
B. Personnel Fringe Benefits (34%)	$127,500	$127,500	$127,500	$382,500
C. Travel	$4,000	$9,000	$12,000	$25,000
D. Equipment	$120,000	$9,000	$9,000	$138,000
E. Materials/Supplies				
F.Subcontractor (CUNY CISDD)	$200,000	$110,000	$110,000	$420,000
G. Other (1st and 3rd year audits)	$10,000		$10,000	$20,000
H. Total Direct Costs from ATP	$800,000	$600,000	$600,000	$2,000,000
I. Total Direct Costs Requested from ATP	$800,000	$600,000	$600,000	$2,000,000
J. Total Direct Costs Shared byProposer	$30,000	$30,000	$40,000	$100,000
K. Total Indirect Costs Absorbed by Proposer	$6,500	$500	$3,500	$10,500
L. Total Costs (Lines H + K)	$836,500	$630,500	$630,500	$2,100,500
2. SOURCES OF FUNDS				
A. ATP (Same as Line I	$800,000	$600,000	$600,000	$2,000,000
B. PI	$30,000	$30,000	$40,000	$100,000
C..PI Indirect absorbed costs	$6,500	$500	$3,500	$10,500
D.				
E. Total Sources of Funds (Same as Line L)	$836,500	$630,500	$630,500	$2,100,500
3. TASKS				
A. 1 Server hardware install and config	$ 412,500			$ 412,500
B. 2 Public client design mock-up	$ 111,000			$ 111,000
C. 3 Program SpiderWeb surface gen	$ 111,000			$ 111,000
D. 4 Recog, sort Crits, Graph display	$ 202,000			$ 202,000
E. 5 Wrie Union/Intersection operator		$ 210,000		$ 210,000
F. 6 Write saddle crit navigator/editor		$ 210,000		$ 210,000
G. 7 Write DICOM, up/down load compres/crypt		$ 210,500		$ 210,500
H. 8 Node warping code			$ 211,000	$ 211,000
I. 9 Write Level of Detail Management code			$ 211,000	$ 211,000
J. 10: Install click stream technology on clients			$221,000	$221,000
K. Total Costs of All Tasks (Same as Line L)	$836,000	$ 630,500	$643,500	$2,100,500

SUBCONTRACTS

1. NAME AND ADDRESS OF SUBCONTRACTOR

CUNY Institute for Software Design and Development
City University Of New York Graduate Center
365 5th Avenue
Room 4319
New York, New York 10016

NAME OF CONTACT: Professsor and Exec Officer Theodore Brown
TELEPHONE NUMBER: +1 (212) 817-8191
FAX NUMBER: +1 (212) 817-1510
E-MAIL ADDRESS: TBrown@gc.cuny.edu

2. TYPE OF ORGANIZATION (CHECK ALL THAT APPLY)

[ ] PROFIT - SMALL BUSINESS
[ ] PROFIT - LARGE BUSINESS
[ ] PROFIT - MEDIUM BUSINESS
[ ] FOREIGN-OWNED U.S. SUBSIDIARY
[ ] NON-PROFIT INDEPENDENT RESEARCH ORGANIZATION
[X] UNIVERSITY
[ ] GOVERNMENTAL LABORATORY

3. ESTIMATED AMOUNT OF SUBCONTRACT

$ 420,000.00

4. DESCRIBE SCOPE OF WORK

Subcontractor will provide mathematical consult, software engineering and codeing services
algorithm design, implementation, and optimization to prime

Subcontractor will provide point of access to CUNY faculty, pay CUNY faculty visiting scientists, PhD students

Providing all fringes, overhead and ancilary costs for pass through by primt to ATP

5. IS THIS A SOLE SOURCE CONTRACT?

[X] YES (IF YES, EXPLAIN) [ ] NO

Justification for Sole Source Contract is based on the expected unique contribution
of the faculty, visiting scientists, and PhD graduate students.

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1. NAME AND ADDRESS OF SUBCONTRACTOR

NAME OF CONTACT:
TELEPHONE NUMBER:
FAX NUMBER:
E-MAIL ADDRESS:

2. TYPE OF ORGANIZATION (CHECK ALL THAT APPLY)

[ ] PROFIT - SMALL BUSINESS
[ ] PROFIT - LARGE BUSINESS
[ ] PROFIT - MEDIUM BUSINESS
[ ] FOREIGN-OWNED U.S. SUBSIDIARY
[ ] NON-PROFIT INDEPENDENT RESEARCH ORGANIZATION
[ ] UNIVERSITY
[ ] GOVERNMENTAL LABORATORY

3. ESTIMATED AMOUNT OF SUBCONTRACT

4. DESCRIBE SCOPE OF WORK

5. IS THIS A SOLE SOURCE CONTRACT?

[ ] YES (IF YES, EXPLAIN) [ ] NO

2 Executive Summary

2.1 Scientific and Technological Merit

CASI (Computer Aided Surgery, Inc.) will develop an application to upload calibrated, encrypted raw images from medical imaging instrumentation (MRI, CT, Ultrasound, etc.), over the Internet. The system will generate precise and accurate, encrypted 3D tiled models with variable Level of Detail (LOD, variable resolution) for applications including: Radiation Therapy (RT), robotic minimally invasive surgery, patient communication, education and other customer applications via the Internet.

Current technology is deficient because it is time consuming, labor intensive, not automatic, and difficult to use. Expert operators produce results for each study that vary, even with the same data reprocessed by the same operator. It is not dimensionally stable or suitably precise for critical radiation or surgical therapy. Extensive hand retouching of the images and smoothing is needed to finish the models. Current segmentation and modeling technology is currently only practiced in research medical centers, and for expensive medical illustration for advertisements.

Competing methods reformat and reorient image planes using *ad hoc* inaccurate methods. CASI's improvement will use 3D surface modeling to rapidly obtain stable measurements delivered via web browser.

2.1.1 Technological Innovation

The novel idea that enables this technological leap forward is Digital Morse Theory (DMT). It describes the behavior of SpiderWeb surfaces by Morse critical features. These surfaces are the computational building tiles of bio-medically important objects. The algorithm indexes all the objects in a volume and segmentation is accomplished by object selection from the index (DMT graph). These novel geometric algorithms will be embodied as a network based application service provider. CASI will function as an Application Service Provider (ASP). This enterprise will function as a computer based geometric foundry for the casting of anatomical structures for biological, surgical, and educational purposes.

CASI will deliver the product models via Virtual Reality Modeling Language (VRML). Customers will manipulate models by mouse, and other virtual reality methods. The click stream behavior of the client will be learned by neural net content personalization technology.

DMT insight enables users to select entire assemblages of components to build desired features without introducing artifacts (segmentation 'tool marks'). With novel mathematical theory, computer graphics programming experience, and clinical research experience, CASI is 4 years to market dominance in high tech medical modeling. We will offer a rapidly delivered, internet based solution for practical patient-specific, tailored requirements, resulting in better diagnosis and better therapeutic quality assurance at mass production costs.

2.1.2 High Technical Risk and Feasibility

The technical risk is that the medical user may have difficulty finding desired objects. For most situations, the object is selected from the DMT graph. In difficult or weak images, additional processing may be required for adjusting contrast and surfaces to suit the user requirements and retain dimensional fidelity. DMT is an innovative algorithm with an unproven ability to solve real modeling problems in a production setting. Common wisdom in the field teaches that volume imaging is the technology of choice for many applications because tiling algorithms make too many tiles, behave poorly with noisy data, and connect extraneous objects therefore confusing the resulting model. Iso- contours and surfaces are used in topographic mapping, meteorology, and other fields, so that there are spillover benefits.

The feasibility of the project is based on preliminary research sponsored by DARPA and results through subcontract with the NIH Visible Human Project (VHP).

2.2 Potential for Broad-Based Economic Benefits

CASI will leverage the large national investment in medical imaging industry by improving image understanding and the quality of decisions based on 3D image stacks. CASI will create new markets for computer biomedical modeling, and propel diffusion of this information to physicians and their patients.

There is an established industry of medical illustration by commercial medical illustrators for medical communication, education, and advertising. The market for patient specific, cheap and rapid anatomic models for critical application will be clearly much larger than diagnostic imaging and medical

illustration. CASI modeling technology, both physical and computer, real and virtual, will benefit the nation by better patient diagnosis, treatment, communication, and teaching. The technology will improve the realization of treatment plans, reduce hospital stays, and enable surgical robot motion planning for minimally invasive surgery, better radiation therapy planning, etc. Patient workups will have the artistic equivalent of an oil portrait by a master painter in the hyperrealism school drawn with the dimensional fidelity of an architectural template. The technology will draw with the accuracy of a micrometer caliper, the precision of an industrial robot, with a reasonable cost, with a market value to the patient/customer in thousands of dollars, with the speed of a Polaroid – Land instant snapshot

2.2.1 National Economic Benefits

The nation will benefit by improved health care that will prolong the quality of life. Reduced employee sick leave will decrease disability related payouts and reduce costs to insurers. The efficient use of medical information will produce better yield on capital in imaging technology. Better patient and physician communication, treatment results, and patient satisfaction will result in less litigation and insurance costs. CASI will create new markets for model-based information as the core competency is established that will go beyond our initial Radiation Treatment project. As the medical imaging industry matures into the medical modeling industry, CASI will seek new markets for services, only dreamed of at present.

2.2.2 Need for ATP Funding

ATP Funding is required because CASI's goal is to make a technical forward leap with the DMT based modeling and develop a business to bring it to market. CASI needs the funding to focus on the production of anatomic models for radiation treatment planning, neurosurgery and medical computer graphics and animations. Building on the NIH Visible Human Project (VHP) preliminary results, CASI will creates new markets that will be profitable within 5-years time. The CASI vision time frame, along with no near term profit projections, is too long for conventional commercial funding.

2.2.3 Pathway to Economic Benefits

This Internet solution will grow explosively, as it is accepted in the state of the art. Internet payment systems provide the infrastructure for direct revenue recovery and interaction with customers. Insurance carriers reimburse costs of 3D reconstruction studies at the two to three hundred dollar levels. The high cost of preparing 3D renderings, and difficulty making critical decisions based on them, had made this unprofitable until CASI.

CASI's intends to become the clinical modeling resource firm. CASI will go beyond medical illustration, becoming a reference standard for dimensionally precise and accurate anatomic models. These will be used for critical treatment applications. The goal is to reduce the cost of generating these models from tens of thousands of dollars and hundreds of man-hours to pennies and the labor time to seconds - literally.

Compared to the established market for high-resolution graphical representations in the medical illustration and advertising industry, there is a much larger market for cheap patient specific diagnostic 3D models.

CASI's first market entry is Radiation Therapy. CASI will leverage many other market sectors by licensing and technical support including direct competitors, forensic image processing companies, histopathology image processing companies, surgical robotics companies, medical imaging equipment manufacturing companies, and picture archiving companies. The state of the art will benefit, in area as diverse as semiconductor process engineering to weather prediction. Any field that uses isosurfaces to understand an underlying physical process will benefit.

3 Project Narrative

3.1 Scientific and Technical Merit

CASI will build a clinical geometry "foundry" casting clinical models in simplicial complexes of triangular tiles that define intricate, real surfaces in three dimensions. Instead of plaster, palladium, or plastic we use surface modeling technology. These models will be used for solving problems as calculating trajectories for radiation beams.

CASI will do this by using a new mathematical theory Digital Morse Theory (DMT) that describes the behavior of isosurfaces. Digital Morse Criticalities are special patterns in the data values where isosurface objects appear, merge, separate, or disappear as the threshold value is varied. These criticalities are, in general, local maxima (Peaks), local minima (Pits), and various kinds of saddles (Passes) in the dataset. By building a list of the locations and values of the Criticalities, CASI software can index (tree graph) all of the objects in a volume data relative to each, in terms of objects that surround other objects (parents), peers (connected by saddles), or are enclosed by other objects (progeny). This index graph is used to enable extremely rapid segmentation and interactively build biologically salient composite surface models from the component isosurface objects.

Further, we will accomplish important image processing and model fusion operations based on matching (registration) images containing common features between models from different imaging modalities of the same anatomic region. We can track and quantify model changes during growth, pathology, and therapy. We can measure several difficult to precisely measure metrics such as surface area, volume, and various moments (center of area, center of mass, standard variability, kurtosis and so on). We can also construct various minimal space curves of trajectories for optimal surgical approaches in terms of Critical Lines (minima and maxima paths between objects), and other applications of computational geometry properties from DMT derived models.

When: We expect to have working alpha prototype systems operating on the web within two years, and beta site clients functioning in four years

We do this because many applications in medicine and the biosciences require a geometric understanding to solve problems at a fundamental level, from which to make critical therapeutic and tactical decisions. These decisions are based on critical dimensions, clearances, access trajectories, and to minimize trauma to no-go regions that must be zealously protected during invasive surgical procedures. The biomedical industry needs patient specific maps, inexpensively produced, with high fidelity for a wide range of therapies. These include radiation therapy, image guided therapy, keyhole brain surgery, minimally invasive robotic surgery, functional modeling of the brain, protein and enzyme kinetics, to cite a few. Engineering solutions to these, apparently simple binary decisions are based on biological morphology from DMT based models are an important problems. The PI's experience in the computational geometry, morphometrics, computer graphics skills, and the insight that DMT provides, propel the PI to make the fruits of DMT widely Internet accessible to physicians and patients.

This project will integrate a range of computer and engineering technologies to connect medical image generators to medical model consumers via web browser based technology. The key to the success is not in the existing technology. Success will be due to the implementation of Digital Morse Theory into a new technology, supported by these ancillary data collection and delivery technologies.

Innovation in computer anatomic modeling technology is by innovation in applied mathematical theory.

Our project is feasible because of preliminary promising results with in the NIH Visible Human Project (VHP) female "Eve" data set[1]. The PI has powerful theoretical results[2] that are just being published in the field. Our business prospects are feasible because of the CASI patent position[3]. CASI has been in business since 1995 as an advanced research and technology research firm, and benefits from the PI's long background in the surgical/medical computer graphics field with publications in the field from 1985

[1] Karron 2001
[2] Cox and Karron 2001
[3] Karron, Cox, and Mishra US Patent #5,898,793

A promising opportunity: The explosion of interest in digital anatomy, virtual humans, visible humans, visible embryos, and even the visible frog project has popularized the concept of computer representations of internal biological and medical anatomy. Two recent Hollywood movies were based on anatomic computer graphics special effects. Multimillion-dollar contracts are being negotiated with computer animation and medical illustration firms for major media outlets (National Geographic and the Discovery Channel). However, the state of the art has not kept up with the demand for much more than pretty pictures and stunning animations. These firms hire a large numbers of technicians to hand segment and retouch manually segmented contour rings from a very large number of slices. Various power assist algorithms are used to reduce the labor intensity of this work, but the size of the raw data sets outpaces the ability of animation staffs to segment, retouch, and render imagery. Computer graphics researchers are developing animation techniques based on this primitive and painstakingly produced geometry. Anatomists spend years developing hand tiled geometric models and animating them. US contractors are failing to meet their milestones and contract deadlines with the VHP data. Firms are leaving the field of medical based animation derived from real data because of the very high costs and long lead times for segmenting desired objects out of pixel anatomic data. Clinical researchers and biological scientists are calling for more data sets of a representative samples of the American population while others are calling for increased resolution imaging of each digitized human. With the potential for a large population of male, female, pediatric, pubescent, adult, and geriatric representatives of each ethnic group, we can expect a very large national sample terabyte scale digital humans. That is one terabyte per sample person so digitized. Clearly, new Level of Detail Management (LOD) technology is required and is a benefit of DMT technology.

This project will advance the state of the art in computer-aided design for biomedical applications, 3D computer graphics, applied computational geometry, rapid prototyping and manufacturing, and robotic surgery. When the PI started this research, the motivation was to produce "correct" isosurfaces for neuromagnetic modeling. Nagging problems with isosurfaces produced by the popular Marching Cubes algorithm of Lorensen and Cline prompted our formalization of a Digital Morse Theory from classical Morse Theory to establish a correct connectivity while moving through all values of iso-threshold. The marching cubes approach is based on a fixed look up table to build triangular tiles in a voxel (defined as boxes with data values at the box vertices). Various fixes to the apparently minor problems in the algorithm are in the computer graphics literature. The flaws were rare, and the frequently invisible in an object with hundreds of thousands of triangular tiles. The fixes solved the problems with small holes in the data in noise by tiling ambiguous cases with a consistent fixed tile orientation. However, for critical measurements and establishing topological, connectivity between objects, in noisy data, isosurface shell models are generally not considered the approach of choice.

The PI's basic research finding was that there are interstitial critical saddle points. The transition in connectivity occurs precisely at that point and threshold value. This saddle depends only on the boxel (2D box element, and voxel face) vertex corners, even for voxels (3D volume element, a 3D cube with volume with data values at the corners). A corollary of this finding is that any fixed lookup table approach to isosurface tiling in the immediate vicinity of a saddle critical point (The so-called "ambiguous" or "4 threshold crossing " tiling cases) results in connectivity errors in general with a probability of _. Saddle critical points are recognized by their characteristic pattern of high/low/high/low vertex values as we circulate around the boxel perimeter. DMT resolves these saddles by subdividing the boxel on the saddle point, effectively changing it into a vertex saddle point. This is different from tetrahedral (or other simplicial decomposition) composition of an ambiguous voxel, because there are still multiple apparently equivalent tetrahedral decompositions. Tetrahedral decomposition moves the ambiguity from the tiling to the tetrahedralization. There is no ambiguity in the DMT subdivided voxel/boxel, as it can never have hits (threshold crossings) on the added subdivision edges. Thus, the orientation of the connections changes relative to the critical value. In this way, as we sweep the iso-value through the saddle critical value, there is only one connection change, precisely at the critical value, and no other value [4] Any other change in connectivity is spurious and causes multiple connectivity jumps as we smoothly sweep through the volume

[4] Karron and Cox 1995

element. Further, the wonderful hierarchical nesting property that Jordan Manifold surfaces exhibit is those we expect in continuous Morse Theory. This important property is destroyed under any other rule set.

The PI believe that other graph based analysis of images in terms of isosurfaces or edge extraction algorithm was not successful because of the faulty nature of the surfaces. Graph based image analysis produced complex graphs that were difficult to understand. DMT graphs are by their very nature hierarchical and rooted in the image/volume.

Spillover Benefits are that isosurfaces are widely used in a number of disparate data analysis situations, *i.e.*, petrology, meteorology, forensic image analysis, hyperspectral imaging, image compression, and understanding. Scientists in other application areas will use our server to build market and problem specific application services. SpiderWeb model scan represent turbulent fluid flow shear surfaces, separation surfaces, cavitation phenomena, and other highly intricate surfaces. SpiderWeb models are noise proof, in that they properly model noise instead of breaking apart or connecting incorrectly. We can represent the relationship between intricate fluid flow structures by the DMT graph representation where computer graphics does not reveal internal structures. We expect that research into many important biophysical phenomena, such as cell membrane porosity, receptor mechanics, and enzyme mechanics will benefit from our tool and analysis. From the preceding list of spillover benefits one can see the contribution to the United States scientific and technical knowledge base, as any application that makes use of surface analysis will benefit by using our technology and ASP.

Project team qualifications; The PI formed the prime contractor company, CASI in 1995. The PI has combined expertise in plastic surgery and neuromagnetic functional imaging dating back to the 1980s (Cutting et al 1986) and advanced mathematical theory in the 1990's (Karron 1992). Our original motivation for geometric modeling was derived from research on neuromagnetic brain anatomy structural and functional modeling. The research evolved into work with cinematic cardiac modeling. The company was founded with a Phase I SBIR Grant from DARPA Advanced Biomedical Technology Grant and went on to do a Phase II grant, and a Phase III add on grant. We also obtained DARPA funding for Digital Morse Theory in the Advanced Computational and Applied Math program at the DARPA Defense Sciences Office. Dr. Karron has run the company web site and ISP since 1995. CASI was founded to be a superspeciality medical surgical ISP. Our web site has been on the air for 6 years, and is well indexed by all of the leading indexing services. This is the basis for our inspiration to run a 'computer anatomic foundry' as an ASP. Dr. J. Cox has been working on the mathematical underpinnings of DMT with Dr. Karron since its inception. Dr. Cox has extensive theoretical and practical experience in new algorithm mathematical description, proof, efficiency evaluation, optimization, and coding in C++ and derived languages. Dr. G Wolberg has many years experience in digital image warping, registration, and is an expert imaging scientist.

3.1.1 Technical Rationale

3.1.1.1 Technical rationale introduction and perspective

The goal is to build surfaces that can be used for object modeling and trajectory analysis. Users will make vital decisions based on the distances between objects, surfaces, and points. Lives will depend on these measurements. Many algorithms and technologies from computer graphics are not of high enough quality for these critical applications. Good enough for graphics display, is not good enough; too time consuming, not repeatable, or too expensive for many important medical applications. CASI requires topological surface tiling make correct connections. Geometric calibrations from the source images must be preserved, and segmentation artifacts (i.e., tool marks) must be eliminated or minimized. Where the image is manipulated, the 'cut' surfaces must be clearly marked so that the user knows what is artifact surface. Hand retouching of objects is expensive, time consuming and introduces additional warpage issues, which reduces confidence on these objects for critical measurements. By preserving calibration at the imaging equipment level, we can precisely and accurately manage warpage and coordinate system disparities between multiple data sources.

Technical challenges that display significant recognized uncertainty of success by experts in the field: Computer graphics and computer modeling are distinct fields. Good enough for computer graphics will not be good enough for our surgical and treatment applications. Measurements of biological shapes are

made difficult by the lack of best practices and standards in the field. This project will help establish best practices for this emerging field. The field biomorphometrics is contentious. Biological shapes require new technology to understand, measure, and manipulate. There are no straight reference edges, circular arcs, or fixed points on which to base a Cartesian coordinate system. Living things are constantly in motion, over time scales of seconds to years. There are a large number of parameters required to describe geometric regions, and no generally accepted theory for a complete description of an organisms shape, much less for diagnostic and therapeutic manipulations of this shape. Industrial metrology is ill suited for such complexities. We intend to extend the limits of the field

Isosurface methods are be used to provide object geometry. However, isosurface methods are not generally considered a preferred segmentation method. This is because previously we have not been able to calculate or visualize clearly exactly, where a particular isosurface object connects to other objects that we do not wish to include in our intended object (the Segmentation Problem). Indeed, the very surface from an object we wish to extract generally obscures the attachment saddle points where our desired object connects to undesired objects. This has been the major difficulty in three-dimensional isosurface based rendering. Other methods, such as volume rendering, are aesthetically pleasing but do not provide geometric rigor and insight required for future analysis and use. Refinements in volume geometry based on volume imaging do not consider topological issues. An algorithm that fit a surface around a cloud of points, or shrink-wraps a minimal area surface around a volume object, forces the topology to that of a single object. It is possible to iteratively build volume image objects into multiple objects, but it is tedious, expensive, and fraught with geometric problems. Unguided isosurface marching geometry runs amuck, covering adjacent objects and obscuring the scene. For critical applications, such as surgical anatomic modeling, we need properly connected surface geometry. Hand segmented objects contain segmentation artifacts, and do not nest properly inside superior and surround inferior objects. New thinking is required to overcome these difficulties without resorting to brute force segmentation by hand drawing slice wise rings, no matter how quickly a professional segmentor can draw rings. There are always going to be too many slices. Artifacts introduced by the illustrator's hand are unacceptable for precise analysis.

There are serious limitations of the state of the art in segmentation technology and theory. Currently, selecting objects in one slice only is a time consuming and frustrating exercise. The partial solution is that the segmentor can see a portion of the object in the image plane. With rapid 2D contouring, the user can quickly find a suitable contour ring from a seed point. This line represents the intersection of a larger surface through the seed slice pixel image plane. We then use this to seed a three dimensional surface. However, the segmentor may find that the surface may have attachments to other objects we do not wish to include in our desired object. The segmentor will need to hunt down the attachment points and do 'something' damming. This is the current state of the art in segmentation.

DMT calculates the connections (DMT Criticalities). DMT segmentation minimally perturbs the contrast at attachment points to achieve the separation we desire. In RGB space, the segmentor may find that there are attachments in one portion of color space, and a suitable segmentation surface exists in another portion of color space. The goal of the segmentor menu is to navigate a segmentation surface through color and other (CT, MRI) spaces; a task 3D interactive computer graphics does not make simple or help visualize.

Isosurface algorithms generally over-tile a surface. Each triangular tile is constructed independently of its neighbor. The size scale of the triangles is less than the voxel size, and in a large data set, the number of triangular tiles can become burdensome to manipulate and display, particularly in real time. The current state of the art is to build a marching tiled surface, then use triangle decimation to collapse almost co-planar triangular tiles into one another. This approach generates large intermediate memory consumption (bloom) of having to build a fully resolved surface then decimate it. This approach, while functional for graphic display purposes, is not deterministic. This means the resultant tiling is very different for every seed tile used to decimate a surface. Decimation changes the geometry of the decimated object in an uncontrolled and possibly unsuitable way.

Digital Morse Theory can provide a solution to these limitations in the state of the art. It can be used as a novel basis for segmentation, data fusion, and LOD management. The technical risks are than that the

algorithm has not been fully implemented, tested, power tested, and accepted in the image and modeling processing community. The algorithm may have computational bottlenecks as we scale up service to production levels on very large images. We ameliorate this risk by using a heavy-duty computer server that can manage large intermediate calculations and memory requirements.

Related topics are hot research on level set theory, isosurface methods, differential equations, and Morse theory. An exhaustive bibliography is beyond the scope and page limits of this proposal, but we refer to the work of J.A. Sethian, Jack Snoeyink, Chandrajit Bajaj, Robin Forman, Stan Osher, John Hart, Carroll K. Johnson, and others. Some of the key theoretical ideas we seeking to develop in medical modeling (Segmentation manipulation by DMT Graph) were explored by C.K. Wall in "Surgeries on Compact Manifolds" (1964, republished 1970, and 1999) by the American Mathematical Society. Marsdon Morse published "The Calculus of Variations in the Large" in 1932. Our principal contribution to the field is the realization of Morse Theory in discrete representations of the underlying continuous world. We make Morse Theory computable. Very recent applications of Braid Theory in Morse Theory have been discussed in applications as diverse as fluid flow and air traffic control avoidance trajectory planning. The intellectual atmosphere is embracing Morse Theory. CASI's computational approach in Digital Morse Theory will have wide applications that we are most keenly aware. Indeed, medical surgery can be considered changing the topology of the patient; Mathematical and computer surgery on DMT object models is the next step logical step in computer modeling of surgical procedures.

3.1.1.2 What is Digital Morse Theory?

Digital Morse Theory describes the behavior of SpiderWeb iso-valued surfaces (US Patent #5,898,793). These surfaces are composed of a simplicial complex of triangular tiles. The surface has the property of being Jordan (no holes). The surface is manifold (no Klein bottles, with consistent normal vectors, a well defined inside and outside). The surfaces within any particular family are "Morseian," (family member surfaces nest entirely inside or outside each other. As we raise or lower the threshold isovalue, the surfaces arise or disappear at well-defined Morse Criticalities. These are kinds of local maxima, local minima, and various kinds of saddles. The surfaces arise from maxima (sources), disappear at minima (sinks), and merge at saddles. Therefore, by scanning through a dataset, we can identify all these component objects by cataloging only the criticalities by their characteristic bit patterns. This is computationally very efficient.

These SpiderWeb surfaces capture essential inflections (transitions from concavity to convexity) in object geometry. Fine scale features (noise) in the geometry create excessive numbers of triangular tiles. DMT provides a method that can reduce the density of tiling by removing smaller through larger scale geometry features in the surface. This is the basis for Level of Detail (LOD) management. For example, if we are using facial features to define a patent based coordinate system, a natural fiducial point such as Nasion (the saddle point on the bridge of nose), can, shift unpredictably in triangle decimation technology. In DMT theory, the larger-scale saddle point remains stable while the smaller, noisy surface features are relaxed smaller to larger, in a hierarchical fashion.

A family of isosurfaces is the collection of surfaces that shares a "one to one" mapping for any point on any member surface to any other such member surface. At Morse criticalities, and only at criticalities, does the mapping property change. This is due to the creation of a new object, the destruction of an object, or the connection to another, object. By showing the Morseian relationship between criticalities (nesting), we establish the relationship between families of surfaces. Because the server can quickly find the Digital Morse Criticalities as bit patterns in the data, we have a new, powerful, and fast way to make topologically coherent, geometrically sound, realizable objects from an image data stack.

A Digital Morse Theory Graph (DMT Graph) is a hierarchical linked list (graph) of all of the separable objects in an image. Each object is identified by its source criticality. We cannot see all of these objects simultaneously because most of the objects are inside other objects, and therefore obscured. Computer graphics does not elucidate the relationship between objects. The hierarchical nature of the DMT Graph is derived from the isosurface families being Jordan Manifold.

There are a number of important practical uses for this insight. We can supply instructions to a rapid prototyping system for making any object or collection of objects in our images. We can rapidly

manufacture fixtures to hold patients precisely and accurately for RT beam steering. Further, we can define optimal paths between these objects, such as minimal distance paths, minimal height paths, or minimal paths subject to some other type of constraint. Constrains surfaces would include maximal avoidance from no-go regions (blood vessels, eloquent brain cortex, or some such vital structure that must not be affected by our surgical robot manipulator). Very recent applications of braid theory to these Morseian paths may be a very efficient method to calculate robotic trajectories and radiation treatment beam plans.

3.1.1.3 The Fish Tank thought experiment: Counting Islands as the water level changes

The essential insight of continuous Morse Theory can be intuited by a thought experiment. Consider a rectangular fish tank. Into this tank, we pour small quantity of sand such that we have two smoothly sloping small hills, one taller than the other. Now, we fill this tank to the brim with water. We now start a count of the number of island objects as we very slowly drain the tank. Our first observation is that there are no island features in our tank scene. As the water level drops, we observe the water level just coincident with the peak of the tallest sand hill. We notice behavior of the water at the critical peak of the hill. We get a degenerate point island contour, with zero area, zero perimeter, and infinite curvature. A vanishing small change in the water level and this point contour expand into a tiny island. We increment our island object count by +1. We continue to drain water from the tank and observe the birth of the second island at the peak of the second little hill. We again increment out island object count by +1 to two objects. As we continue to observe the drop in water level in our tank, we observe the two island contours expand and grow toward each other. As the water level reaches the level of the critical saddle point between the two hills the island contours touch at precisely the saddle point. We observe that our object count decrements by –1 to give a total island count of one. The essential feature of this rubric is that we only need to count the peaks and passes to inventory all of the object islands in our scene. This approach works even as we increase the complexity of the scene. We can use the same idea of enumerating peak, pits and pass criticalities in a very complex archipelago of island features, at any size scale, or any range of size scales, including noise at any size scale.

3.1.1.4 Why a Digital version of Morse Theory?

Morse theory works precisely because it solves the problem of singularities in data models. CASI will use its digital version of Morse Theory that works on computers with pixilated data, which will yield the same results as continuum Morse theory on analytic Morseian functions. Digital Morse Theory extends Morse Theory to discrete data, such as a digital image. Digital Morse Theory describes the behavior of SpiderWeb surfaces and objects. There has been significant research effort to build quickly computable surfaces. There is little work on technology that effectively describes all of the isosurface objects in a volume data set. No research provides a practical method of indexing all of these objects in a useful and comprehensive fashion. In order to make Morse Theory work in this digital setting, DMT adapted the notion Peaks, Pits, and Passes in subtle but important ways. We extended the idea of a Peak to include not just a point peak or pit, but plateau peaks, and pits. Criticalities can also be ridges, extremum of curvature, and umbilicus of curvature (a curvature saddle). Saddles had to be extended to include not just vertex saddles (where the saddle point is collocated on a vertex) but also the most common interstitial saddle point. This solved the so-called problem of "ambiguous" voxels. This means that the surface is completely determined, unambiguously tiled, and stable surface representation in any texture or noise.

3.1.1.5 Digital Morse Theory for rapid effective semiautomatic segmentation

The eye sees interesting objects in a 2D image and the mind would like to reach into the image and isolate (segment) that object from the surrounding pixels. If the 2D image is a slice through a stack of slices imaging a 3D volume, we can attempt to segment the entire object from the surrounding voxels, including the unseen portions above and below our planar sub-sample. If we are lucky, we can use 2D isocontours lines to estimate 3D objects. The current state of the art in segmentation is to select a seed location and use that seed to start propagating contours lines in the reference image plane and contour surfaces in the volume image stack. The problems arise where we have a likely looking contour ring object, and use that to seed a volume object surface. What may look appropriate in one slice will frequently run amuck and connect inappropriately to other extraneous objects in other slices. The segmentor needs some guidance as to where the object that we wish to segment in any one image slice will connect to other objects anywhere in the

volume image stack; including the currently visible slice, and/or in slices above or below. To make matters worse, the very surface we are seeking to grow obscures the critical features where it connects to other objects.

The current state of the art is to build pixel fences of higher valued pixels to constrain a growing surface. This is a modified kind of image retouching. We are attempting to retouch not the object, but just a vanishing distance beyond the objects' borders. It is retouching almost blindly, in hope that we are corralling our emergent surface appropriately. A lot of fencing may be used in a complicated object. While not all fence objects are required, they will change the shape of the object in the immediate vicinity. In order to guarantee that our surface won't leap over the pixel fence, we have to use a very high value, typically fully saturated white values at the upper end of the image histogram. By raising a high fence around the object, we are changing the strength of the surface. The strength of the surface is the intensity of the gradient normal to the surface. A surface can be weak if the delta intensity crossing from inside to outside is very small, or an identical surface can have a very large intensity change across the threshold valne. The only way the surfaces can be independent of the strength of the surface is for the strength of the surfaces be identical at all points. Therefore, any uneven changes in the strength of the surface (which would result from hand carving or hand fencing by changing pixel values) would introduce geometric changes in the surface that we have dubbed 'tool marks'. Typically, these artifactual features are removed by post processing operations to smooth out rough spots. This makes using this technology for modeling expensive, time consuming, and requires an expert operator.

Edisonian invention vs. Advanced Math Insight: The state of the art in image segmentation is trial and error, cut and fit, iterate, and refine; reminiscent of Edison's attempts at managing the voltage drops in the early DC power distribution grids. Edison built scale models of the grid with copper wire, and measured the voltages the subscribers on the grid would see. A young scientist came to Edison looking for a job, boasting that he could calculate the voltage drops without trial and error estimation. Edison needed a hard worker, but resented the hubris of the man. Eventually Edison eventually threw Telsa out. DMT afford a way to directly map/graph the objects in a data volume at every threshold, without browsing or exploring the volume with 3D interactive computer graphics. CASI will move tbe state of the art out of Edisonian segmentation and into the deep insight that DMT provides; an application of advanced math to solve a multi-industry problem.

3.1.1.6 Decomposition of pixel image into DMT graph representation

The DMT graph is the first step in the analysis of an image in terms of its surface defined objects. All objects are composed of various implicit isosurface objects. This graph representation is a hierarchical index of all of the component objects in the data volume. Additional information can be encoded into the graph with the geometric shape information of each implicit object. Essentially this operation recodes the image intensity information into a system of peaks, pits and passes organized into parents, peers, and progeny (the PPP to ppp relationship). Further, each component of the object shape can be further graphed as a system of concavities, convexities, and their umbilici (the region between where the surface passes through flat. Since each object is a closed, manifold, this enforces the surprising and useful parent to progeny hierarchical organization. DMT analysis effectively turns a pixel image into a vector drawing in terms of contour line and simplicial triangular tiles.

3.1.1.7 Application of Union and Intersection operations to establish homology between images

Because each related images is a rooted tree graph, we can start matching trees by various graph-matching algorithms we will be designing with our computational geometry colleagues at the CUNY. Our algorithm design approach is based on the idea that the root of an image graph contains all of the area of the image. Each node under the root contains a normalized fraction of the image area relative to the whole of the image. In this way, the DMT graph is a completely dimensionless representation of an image in terms of area/volume fraction and Morse criticality a union image graph is all of the common image features between two related images, such as an MRI and a CT image. It is calculated by recursive descent searching into each node, then sub node. The intersection image is all of the independent features not common between two images. The novel applications of such a graph will be among the most exciting and useful new finding expected to come from this research. We believe that the brain uses this approach for steriopsis

and the synthesis of range information from two related points of view. Previous efforts at image graph decomposition were confusing and generally considered not fruitful. Because the SpiderWeb surfaces are Jordan Manifold, they decompose naturally into a tree graph (because the surfaces don't interpenetrate and join only at critical nodes), and the results are natural to understand.

3.1.1.8 Medical Illustration and Medical Modeling

Medical illustration is the communication of a medical concept from the mind of the artist to the mind of the viewer. It is intended as an educational process, not necessary as data display and analysis. Medical Modeling, as we wish to compare and contrast against, is the technology for the building of geometric models of anatomic features. Without suitable tools for the segmentation and modeling of geometry from medical images, medical modeling can become medical illustration using three dimensional computer graphics because of excessive hand retouching and smoothing. While computer graphics is an important part displaying our computer anatomy, computer graphics is not the product and imaging it not out intention. We consider this a biomedical engineering project. However, we recognize that there is a significant need and highly profitable market in medical illustration and animation industry that we can serve and derive a significant revenue stream. This is because our technology can reduce the extreme costs of preparation of high-resolution anatomic images and animations significantly.

3.1.1.9 Computer graphics and the curse of dimensionality

As technology provides us with more raw data channels, at faster rates, at greater resolution, our ability to comprehend it is limited by our ability to visualize it in three dimensions, in three primary colors, interactively. High-speed interactive computer graphics, and advanced rendering algorithms, require slow, careful, and expensive examination of the spatial nature of the data by a dedicated expert. Each channel of information may be dependent on each other. Additional resolution may not increase our understanding of the relationship between objects. We need new ways to understand higher dimensional data where computer graphics overwhelms the visual system of the observer, or requires extensive interactive exploration, observation, and analysis of an expert operator. As technology give us more channels of data, computer graphics can compound the "curse" of too many dimensions of data.

A DMT graph based topological understanding of complex higher dimensional (Color, CT, MRI, PET information dimensions) spatial relationship is our proposed "cure" for the "curse" of higher dimensional data channels. This is because a topological relationship can be represented independently of the dimensionality of the data; A ball in 3-dimensions is one node on the graph, as is a ball in 20 hyperspectral colors.

3.1.1.10 Description of technical challenges and barriers we will tackle

3.1.1.10.1 DMT for image segmentation

Segmentation for precise and accurate application requires the segmentor make no, or minimal changes in the image. For many images, we only need to find a path (segmentation plane) around an object. Where none exists, we need to 'carve' one. We require well-defined minimal 'surgical' changes in the image such that we minimize warpage in the resultant objects' geometry. We define a 'DMT Segmentation Operator' to manipulate connecting saddle values to enable wholesale connection or disconnection of objects; effectively carving (separating) and gluing (joining) objects with single mouse clicks.

In noisy data, or when segmenting in uneven difficult geometry (blood vesicles, nerves, thin bone), in order to separate an object multiply connected to its proximate objects, we have to introduce additional contrast to separate the desired object. We can restate the problem; what pixel locations with what value changes need to be applied to achieve the separation we specify. We employ a contrast mask image layer, to preserve the original pixel data values. Using the DMT graph, the user select the most proximate saddle nodes and applies the 'segment' operation to elevate or depress saddles as required to parse an object from its neighbors. We then mark this 'cut' surface so that we are aware that this is an artificial surface. As we make only the minimum changes in gradient, we minimize the introduction of 'tool marks', and maximally generate a smooth cut surface. Preliminary testing of this procedure has been most promising.

3.1.1.10.2 DMT for image registration

Image registration is any of a number of methods that translate, scale, and rotate an image such that common features in both images are made to be co-incident. The determination of the common features, or

homologous points, lines, and regions, is typically specified by a technician's eye. The popular animation effect of morphing one (somewhat) related image into another image requires a lot of human interpretation to specify which points and image regions are to be warped into another. An important application in medical imaging is the combination of multiple imaging modalities into one image representing the fusion of features between both images. Manual determination of common features, particularly in cinematic medical image series, can be time consuming and expensive. Automatic or semiautomatic methods are needed. Digital Morse Theory provides a new means of image understanding to identify common features between one or many images.

3.1.1.10.3 Registration of images by DMT union operators and digital image warping

The goal of registration is to recognize homologous features in disparate view of the same scene. Decomposition of disparate images into DMT graphs is the approach for this project. An example would be calculating range information from two closely spaced Point of View (POV) images, or varying the MRI pulse sequence progressively from one sequence to another. At very small POV disparity (in distance, or pulse sequence), we increase the disparity between the two images. We will conduct experiments where we continuously calculate the DMT scene graph from two views with increasing disparity between the views. Our aim is to validate algorithms for calculating the DMT Union and Intersection graph. With a validated algorithm for calculating the Union between two scenes, we can do fully automatic registration between scenes and solve an important problem in image fusion, automatic steriopsis, and the CASI modeling service.

We can register disparate but similar images by calculating the common features of the images (union) without the disparate features (the intersection of the images). From the union graph, we can calculate the digital affine transform required to match each homologous node to occupy the same space (An affine matrix at each Morse criticality node). We can then apply the intersection image at each parent node to generate a topologically correct but warped to fit the union fusion image that is geometrically calibrated by one of the images' calibrations.

3.1.1.10.4 Bandwidth management

DMT based representations can be used to transmit an image from large features to progressively smaller images. This will be an important spillover benefit, in that we will be able to send images efficiently through limited bandwidth by organizing the image for transmission from largest to smallest component. We will be able to transmit a pixel image without drawing any pixels. We will transmit the image as large component contours first. Successively smaller and smaller contour objects will build on the client web browser, but the essential geometry of an image will build in the first data packets of the image. We will draw the vector geometry of pixel images at significant bandwidth savings. That way the image will more quickly recognizable very early in the image build process. Optimized picture transmission over the web important for sending images echoing clients data back down to clients browser.

3.1.1.10.5 Trajectory planning for surgery: Braided Digital Morse Theory

The state of the art in Surgical Robotics is remote actuators with video and/or haptic feed back. A true robot has some algorithm and model about the environment it is attempting to navigate. Improved algorithms for navigating inside the body are required which need models from which we can calculate internal trajectories. This is a technical challenge we believe we can tackle in this project because we can calculate optimal paths between criticalities. Between two peak criticalities, there must be a saddle criticality. New Variational Calculus and Morse Theory methods can provide a "least distance" or "minimum height" path between the two. We will research new concepts in Braid theory applied to DMT (Braided Digital Morse Theory) with Braid expert Professor. M. Anshel.

3.1.1.10.6 Trajectory planning for Radiation Therapy Beams

A particularly difficult tumor location to treat with radiation or electron beams is the breast. The goal is to destroy the cancerous tissue, which may or may not be a well-defined mass inside the breast, overlaying the thorax and in dangerous proximity to the heart and lungs. Patient fixation and re-fixation during the course of radiation therapy is difficult. In the current state of the art, it is expected that collateral damage be inflicted to the heart and lungs during high-energy breast RT. CASI and its clinical collaborators at NYUMC believe that with better modeling of the breast, the tumor, and the thorax, we can design better

therapies. RT requires serial models the tumor during the course of therapy. CASI will be able to build models of critical organ geometry, design fixation jigs for the patient, and beam trajectories.

3.1.2 Assessment of success of the project approaches and alternatives

Our assessment of the success of this project is based these positive and negative features of our proposal:

3.1.2.1 PLUS

We have a comprehensive new theory that solves important problems in the state of the art in a number of fields. The theory is proven, and based on classical Morse Theory, and is a hot research topic (Braided Morse Theory, Level Set Theory, Contour Trees). The principals and faculty are world-class graphics programmers, applied mathematicians, expert in algorithm design, optimization, and complexity analysis, expert in ISP and web site management, and the DICOM Imaging Instrument interchange standard. The PI's preliminary results with 2D RGB (color) Visible Human project data are encouraging.

3.1.2.2 MINUS

The utility of our new algorithms are not established in surgical or radiological practice. The software is written as academic demonstrations and proof of concepts only. Significant work is required to make the applied math solve our customers problems. We need to educate technologists and professionals in the field, as DMT graph segmentation is based on a new paradigm. Technical superiority of a new algorithm alone will not necessarily lead to widespread acceptance. The delivery of a solution and the ease of its use can be more important to market adoption.

We must understand the biology as well as the anatomy of what we are modeling. Using only anatomic imaging to attempt to pin down issues of precision, accuracy, in a living, highly variable, perverse human population is going to fail. Intraoperative visualization is the way to get geometric feedback for accurate geometric placement, but it will not necessarily improve patient treatment results. Functional imaging may show that the source of pathology is not at the center of the anatomy. Functional imaging (functional MRI, volume impedance tomography or neuromagnetic source imaging) will ultimately be the solution. CASI DMT can manage issues of precision and accuracy in data fusion between widely disparate resolution scales typically found in functional images fusion. The biology of the pathology will most certainly complicate the geometry in novel and exciting ways.

3.1.3 Implementation details rational

The main interface to the CASI system will be by connecting to the CASI web site at http://www.casi.net/ and logging in via a secured socket level connection, with all image and model transactions encrypted to the appropriate privacy standards for patient information (HIPPA). There are two fundamental operations on the server. The first is uploading raw image data and then generating the topological decomposition and recoding into a DMT graph. The DMT graph indexes each object in a volume, and each feature in the object geometry. The graph of a volume contains the same information as the pixel data; but in a hierarchical segment able object format. The second fundamental operation is tiling from a node on the DMT graph. The model is created at a bandwidth appropriate tile density and downloaded to the user. This is possible at interactive speeds because the DMT graph is an index into the volume, enabling rapid segmentation and model generation.

The model server is the heart and soul of our effort, the "forge" through which pixels become anatomy. Raw image stacks are uploaded. A DMT graph is presented back to the user. As the user moves the mouse, tiled models are forwarded to the client for real time interactive approval or further pick, drag and drop assembly.

The radiological client user will log into their account at CASI, on a client machine on their local network, which will also connect to the imaging equipment via the radiologist facility TCP/IP net to a DICOM (Digital Image Communication) protocol for interchange of medical images that runs on all medium to high end medical imaging equipment. Each radiological facility will provide access to its imaging equipment image files. We will write code that will enable the client to push the code up to the server, or the server will be able to automatically pull client images as they are produced. The images and associated patient identifying information will be encoded and encrypted to HIPPA (Health Insurance Portability and Accountability Act of 1996.) Software features are a universal file and directory recognition

system, that can learn the format of any medical imaging instrument file format, and any popular digital image format so that installation in a client radiological site is quick and trouble free. We will also build a universal calibration service into the radiological client. Most imaging equipment has maintenance contracts and quality assurance requires that the equipment be calibrated by imaging an imaging phantom with known geometry and dimensions. We propose to provide a uniform calibration service to insure uniform model fidelity for all of our client images. In that way we can provide a cross instrument, cross instrument manufacturer, calibration standard so that our geometric models are of well defined quality, independent of the standards of instrument care the client maintenance standards call for, and meet CASI defined standards.

The design goal for the referring physician client software is to have immediate access to the imaging study and minimize the work required to do a three-dimensional work up. The referring physician, the attending surgeon and any of the consulting caregivers authorized by the referring physician, can access the images, the patient models, and any study tools, annotations, and other material. This may include medical illustrations, reference materials, annotated treatment plan models, pre, post treatment photographs, intraoperative photographs, and so on. The materials may be to educate the patient as to the upcoming procedure, document the procedure plan, report the procedure results, or even sell a prospective case to an uncertain patient. Because we are going to be doing interactive three-dimensional computer graphics on the downloaded anatomic models, we will enforce a minimum level of graphics resolution and triangle rendering speed by the client. These standards are approximately the same as available in any high-end computer video board with OpenGL support. These boards cost approximately 100 to 1,000 dollars with a polygon draw rate of at least 30 million illuminated, z buffered triangles per second. This a standard value for a PC workstation class graphics accelerator board, or a high end computer game OpenGL board

The patient client software can display study models permitted to the patient by the referring physicians' client. This is a limited functionality physician interface. In this, the physician can educate, inform, or sell the case to the patient.

We will use VHP RGB data and register the base anatomy to the CT and MRI patient specific images. We will build detailed models that contain the diagnostic information particular to the patient. Our goal is to generate a fused composite model of the patient, containing standardized anatomic data scaled and registered into the patient coordinate system, to provide color and other inferred structure detail that MRI and CT do not measure. As we validate our code, and the radiology facilities client code approaches completion, we will move to using patient specific MRI and CT source data.

Level of Detail (LOD) management is key to the commercial success of this project. The models, as built on the server will be over tiled (have more triangles than required to solve most modeling and trajectory problems). Delivery of the product models and images to the client computer must be appropriate to the available client bandwidth, display resolution, and the client computer storage capacity. Interactivity requires rapid LOD management so server downloads only enough detail to permit the client computer to display the model on its OpenGL graphics accelerator subsystem. Failure to achieve the desired bandwidth and latency by the project termination data will be offset by the expected growth in next generation Internet bandwidth and yet even faster graphics chip sets. Should hardware technology obviate the need for an extensive LOD management subsystem, we will scale back our effort in this area appropriately.

We will close the loop with our users by installing a click stream subsystem to monitor how our users interact with the selection/segmentation menu. From are able to optimize the interface to minimize the selection, and segmentation clicks required of our users. Selecting objects can require a lot of picking and selecting on a deep the DMT graph menu. We expect that most users will make canonical selections, and by monitoring patterns in the selection behaviour, we believe we can intuit users intention, taste, and desired objects after they make similar choices in different patient datasets. As our system gains experience with alpha testers ad users, we will test to see if this facility makes using our system intuitive and decreases each users number of selection clicks to find the models they wish. In this way the user interface and the speed and quality of the users' modeling effort is improved.

We will build a Radiation and Oncology Physician Client Interface that implements special features requested by our Radiation Therapy (RT) collaborators at NYUMC. We will use our core technology to segment and build models, but also track successive tumor model changes during treatment, develop beam

trajectories (via Braided DMT) through the target (the breast tumor) and no-go regions (the lungs and heart). We will develop ablation isodose isosurfaces (surfaces of dosage intensity great enough to ablate tissue), and low dose isodose surface (the surfaces of dosage intensity safe for healthy tissue), for no go region. We will build union and intersections of these organ and isodose objects using our DMT graph technology to highlight dangerous problems before the patient is hurt, and to validate treatment plans prior to treatment.

We will begin by doing breast cancer cases using the generalized physician client with the radiation oncology department at NYUMC. We will be building patient models from CT slices, and modeling tumors during the course of treatment. We will also develop isodose surface maps of total radiation absorbed as well calculating beam trajectories. Our goal is to minimize the radiation dosage in the thorax and maximize dosage in the targeted tumor. The research challenge is to do difficult beam trajectories that the department software cannot manage because of the geometric complexity or lack of critical organ models.

We will build a Neurosurgical client interface, to provide steriotactic brain surgery planning for keyhole surgery. We will incorporate features requested by our Neurosurgical colleagues at St. Louis University (SLU). We use our modeling technology to build no go regions such as articulate un-diseased brain and major blood vessels, and the target region we wish to biopsy, ablate, or deliver therapeutic agents. We can model the union of the no go regions and the access path to validate surgical plans prior to surgery. Any volume in that object class will immediately flags a problem.

3.1.4 State of the art before project:

The current state of the art for anatomic modeling is hand pixel picking or semi-automatic power hand assists (snakes, dilation / erosion operators, flooding regions, etc.), drawing contour rings, sewing a surface between rings. Marching cubes and friends tiles all objects at a threshold value, regardless of their connectivity. Various advanced techniques require hand drawing pixel "dams" to contain surfaces from spilling into inappropriate regions, or "roughing in objects" prior to contouring. These techniques distort the object geometry, are imprecise, create tool marks, and other dimensional instabilities. They require an expert operator, are not repeatable, even with the same operator on the same data. Critical radiation therapy simulation modeling for beam trajectory planning is done by the seat of the pants, line of sight, with insufficient computational geometry support on physical simulators. Robotic surgery is not; there is no theoretical, robotics technology to makes calculation of intraoperative trajectories possible without good anatomic modeling. Currently, neurosurgical trajectories are typically simple straight lines avoiding large internal obstacles (blood vesicles or eloquent cortex). Anatomic computer animation for medical or commercial illustration requires many technicians working on multiple packages doing hundreds of hours of hand editing to make seconds of finished rendered animation frames.

3.1.5 State of the art after project

Within three to four years from the start of this project, segmentation will be accomplished in seconds; simply by moving a mouse over a DMT graph (specifying a threshold value and parent criticality) browser widget, and immediately seeing the 3D object selected. If the object is not simply selectable (the desired object is has multiple connection nodes to other objects), the user can click on the graph node to have the proximate connecting nodes disconnected by changing the minimum number of pixels the minimum contrast. Surgical robots will use real time updated anatomic model information to navigate deep inside the body. Difficult to reach breast tumors will be treated with no burnt lungs. The segmented models will be precise, accurate, and suitable for Hollywood computer animation, deep brain surgery, and high school student science fair projects. The technical leverage of understanding surfaces, objects, and being able to manipulate them adroitly are manifold. Any engineering or scientific application that typically uses isosurfaces for analysis will benefit from DMT graph analysis.

3.1.6 Technical leverage into a broad spectrum of spillover benefits

The technical leverage of understanding images, surfaces, objects, and being able to manipulate them adroitly are manifold. We will be able to effectively transmit large pixel images as nested large to small contour objects. Any engineering or scientific application that typically uses isosurfaces for analysis will benefit from DMT graph analysis.

3.1.7 Technical Rational and Advancement of the State of the Art (TABLE)

Figure of Merit	Projected Technical Targets	Current State of the Art	Technical Barriers	Innovative Approach
Resolution (Distance)	No Resolution Limits	1/3 mm pixel size	Scanner device pixel size, typically, imaging devices produce too many pixels to use all of information effectively	Vector from pixels
Effort (Time)	1,2 seconds, possibly interactive speeds (1/30th second)	Hours, days, weeks	Patience of operator, excessive resolution of image data. Objects to be extracted require specifying every pixel, or every perimeter pixel.	DMT Graph specified objects are hierarchal, so groups of objects can be manipulated instead of individual pixels. Single mouse clicks segment complex objects
Cost of Professional Effort	200.00 to 500.00 / man hour	10.00 / man hour	Low productivity of current algorithms and software	
Accuracy (Standard Deviation Distance)	< 1 pixel	> 4 pixels	Segmentor technician hand work; Movement of patient during surgery, time interval from imaging to treatment cause measurements drift	Rapid modeling minimizes changes due to time delay from imaging to treatment. Real time intraoperative modeling possible
Patient Results (Percent Improvement)	95 %	45%	Precise determination of pathology location	Accurate and precise modeling preserving imaging calibration

3.2 Research and Development Plan

3.2.1 R&D Plan overview

The development strategy is a simultaneous attack on the math and implementation problem; algorithm design, and software engineering problem. The principle division of tasks is between the user interfaces (client side Java development) and the DMT image recoding, graph generation, union and intersection matching, Level of Detail (LOD) management, bandwidth management, and warping tasks (server side math and remote graphics). The PI will program the DMT decomposition and graphing code. A core algorithm research and programming team will be assembled from the faculty and PhD student pool. Dr. Wolberg will program manual and automatic image registration. CUNY faculty will do algorithm development and analysis. NYUMC RT and SLU Neurosurgery faculty will be our alpha clients. PhD students with Java and C++ experience will program the client side browser plug-ins. The math research milestones are the development of the server image graphing, matching, registration, and LOD management. CASI will launch its alpha test network based client-server image-processing services directly to the public, to imaging facilities and physicians (and their patients) even before all of the server services are functional or complete. By having the client technology base working, even at mock-up prototype functionality, CASI will transition research milestones rapidly, effectively, and explosively diffusing the technology into clients' lap (tops).

3.2.2 Technical Barriers Overcome by CASI that will yield Economic Benefits (TABLE)

Technical Barrier	New Technology	Economic Benefit
Extensive, expensive human segmentation by pixels, hand drawn contours, hand drawn pixel dams, segmentation snakes, and other current ineffective technology: Imprecise and Inaccurate	DMT critical point manipulation precisely segments objects.	Creation of new market low cost computer modeling Cheap patient specific graphics and animations,
Smoothing operations on hand segmented objects: Warps object geometry	Maximal smooth 'cut' segmentation surfaces	Reduced dependence on student and technician for retouching and smoothing
Dimensional Fidelity of segmented, smoothed objects: Inability to preserve of instrument calibrations from image to model		Increased market in patient specific imaging and modeling,
Robotic Surgical Planning: no technology to calculate in patient specific model anatomy; no way to model constraint space (no-go regions); no way to calculate optimal trajectories	Braided Digital Morse Theory for paths between features	Better surgical results, Less insurance costs, Lower hospitalization costs, Less hospital time, Less disability payout, Increased worker productivity

Radiation Treatment Planning: inability to get precise and accurate simulator models; no technology to calculate optimal beam trajectories subject to constrain spaces (no-go regions):		NO surgery required, Better treatment results, Less insurance costs, Reduced hospitalization costs, Less disability payout
Treatment Results Evaluation: repeated hand modeling of tumor or target organ during therapy too expensive, imprecise, and labor intensive	Reliable tracking of tissue morphological changes from radiation or surgery over time	Quantitative measure of treatment effect (Tumor volume shrinkage, qualitative morphology improvement, etc)

3.3 Statement of project tasks and anticipated accomplishments

3.3.1 First year project milestones

For the first project year, we will focus on algorithm development and implementation to efficiently produce and manipulate the images and models by their DMT graph node. Concurrently, the client side interface team will design, mock up, and write browser-based interfaces for our intended medical imaging shops and clients. This will demonstrate of DMT principle of producing map of objects that do not require contrast enhancement to be parsed out of their proximate objects. We will boot up our network services server on the Internet.

3.3.1.1 MILESTONE 1: Server live on Internet

We will launch our project with the purchase and configuration of the CASI project web site server.

TASK: install the project management software, and establish protocols for collaborative programming with the team members.

3.3.1.2 MILESTONE 2: Public client mock-up facility life on Internet

Publish concept mock up our system into which we will insert the real functionality as that milestone is achieved.

TASK: Design various user interfaces for radiological, RT, Neurosurgical, patient and public use classes.

3.3.1.3 MILESTONE 3: Surface tiled models from DMT graphs

Generate a tiled surface model in RGB Color image data from a user selected threshold value and a DMT graph node.

TASK: Program SpiderWeb algorithm and DMT graph decomposition

3.3.1.4 MILESTONE 4: Generate DMT graph from image stacks

Generate DMT Gray scale graph from MRI and CT from the VHP. Generate DMT graph of the color (RGB) VHP pixel data. We will use the female 'Eve' data set, and do the thorax and abdomen.

TASK:

3.3.2 Second year project milestones

The second year of the project will focus on the DMT segmentation operator and registration, then delivering them into network clients.

3.3.2.1 MILESTONE 5: Gray scale and RGB Image graph matching (registration precursor)

We will build the union graph of the RGB and one or more of the CT and MRI image stacks for manageable subset of the VHP data.

TASK:

3.3.2.2 MILESTONE 6: Segmentation functionality demonstration

Using the public VHP data, we will demonstration on the website DMT graph selection of component objects. Users will select DMT objects from the RGB, CT, or MRI data sets. DMT segmentation operator demonstration, by clicking on the DMT graph node, the user will move saddle connections up or down to connect or disconnect objects.

TASK: Write saddle criticality navigator (finds segmentation plane if possible), else edit saddle values to edit DMT graph edges.

3.3.2.3 MILESTONE 7: The Patient, RT Physician and Steriotactic Neurosurgery Client demonstration goes live

TASK

3.3.3 Third year project milestones

CASI focuses on the problem of object registration and delivery of reduced density images and models.

3.3.3.1 MILESTONE 8: Registration of models by DMT graph demonstration

We will demonstrate the union and warping of DMT graphs from selected subsets of each data set resulting in a fused model.

TASK:

3.3.3.2 MILESTONE 9: Level of Detail management 10-x reduction in tile density

We will demonstrate a minimum of 10-x reduction in tile density, with a maximum reduction of tile density of an object into a tetrahedron (4 triangular tiles).

TASK:

3.3.3.3 MILESTONE 10: Segmentation click stream learning captures segmentor insight

We will demonstrate a 10x reduction in the number of clicks to segment major components by learning patterns that will enable us to intuit objects to segment.

TASK:

3.3.4 MILESTONE PROGRESS (TABLE)

N	Major Project Tasks	Project Time Y1	Y2	Y3	Cost in $K	Major Milestone
1	Server hardware installation and software configuration task	■			412.5	Server live on Internet
2	Public client mock up facility design task	■			111	Public client mock-up facility life on Internet
3	Program SpiderWeb surface tile generator task	■			111	Surface tiled models from DMT graphs
4	Recognize, sort Crits, connect graph display code task	■			202	Generate DMT graph from image stacks
5	Write node figure of merit, sorting, matching code for Union and Intersection operator		■		210	Gray scale and RGB Image graph matching (registration precursor)
6	Write saddle Crit navigator and editor		■		210	Segmentation functionality demonstration
7	Write DICOM, upload, download compression, encryption, radiological, referring physician client		■		210.5	Web based upload and download of raw images and tiled models
8	Node warping code			■	211	Registration of CT and MRI to VHP Base Anatomy
9	Level of Detail Management			■	211	Level of Detail management 10-x reduction in tile density
10	Install clicks stream technology on clients; collect data from alpha users			■	221.5	Intuiting segmentation from users

3.4 How will our project handle technical and managerial problems we will encounter

3.4.1 Computational load problems in larger scale image stacks

There may be complexity issues as the images scale, the number of image dimensions increases (independent or dependant image channels). Scaling up to a production system may overload the server, or increases in image resolution in future CT and MRI systems may similarly overload the server. Interactivity may suffer. The NP completeness of these algorithms has not yet been analyzed. Software optimization as well as new capital to buy a larger server may required as we process more and larger alpha client datasets.

3.4.2 Computational intermediate solution memory "bloom"

Registration of large images with disjoint area may cause problems. If the two images have the same borders, then the root of the graphs will be the same and graph matching can start at the same depth levels on each graph. If the two images are disjoint, i.e., there is only a small common area between the two images, and then the graph-matching algorithm will exhaustively search for matches in the regions where no such match is possible. This unproductive searching may cause problems with excessive temporary memory requirements. Images that have no common features may produce spurious matches, perhaps matching textures and small features only, while assigning most features to the intersection list

3.4.3 Automatic registration problems: managing matching incomplete graphs

An incomplete graph is a graph of a portion of the object that we wish to register. It is important we start with a complete view of the structure we wish to register, but the algorithm should be able to find the best matching node tree segment by exhaustive searching.

The worst-case situation is that automatic graph matching cannot be made to work fully automatically to our satisfaction. In that situation, and until we can design a fully automatic graph matching algorithm, we will ask users provide a starting point on graph pairs to the matching process.

3.4.4 Segmentation of difficult images

A difficult image is an image that contains features that distort isosurfaces on a large scale, and or fine grain noise that causes a very large number of small noise objects. We can eliminate small-scale features by truncating our graph below an object size, typically on the scale of two or four pixel lengths. Large-scale distortions include bright MRI antenna fields, a 'tilted' image background, where the image is distinctly lighter on one side, and darker on another side. Other problems we have encountered are bright 'hot' spots produced by MRI pickup antennas placed directly on the patient to improve image resolution in the immediate vicinity. This causes an intense detailed and bright hot region whose brightness decays away from the antenna. For those images, we have to model and brightness compensate the antenna field.

We are prepared to do additional traditional image processing, even hand editing, as part of our technical assistance to the user, until we can design and implement automatic methods to minimize this kluge step. This experience is a necessary and unpredictable part of dealing with real images that we expect from our clients.

3.4.5 Management issues

Access to necessary research facilities by proximity; We will have access to offices of the City University of New York (CUNY) Graduate Center (GC) on 34th street and 5th Ave, a short distance from CASI on 33rd street and 2nd Avenue. Team programmers will have the option to work directly on the machine for very fast image rendering, and manipulation, or work from PC clients on site or remotely. Clinical collaborators are all well Internet connected, and mainly at New York University Medical Center (NYUMC) on 34th Street and at St. Louis University (SLU). As we move from computer modeling to clinical modeling, we expect to be working extensively on site at the Radiation Oncology facilities directly across the street from CASI. The PI has many years standing as former faculty at NYUMC and collaborations there are easy to negotiate as required.

3.4.6 Fostering a team approach and team member communications

3.4.6.1 Project Management Policies

We will establish a simple task delegation and completion policy, as well as regular weekly face-to-face meetings at CASI and at the CUNY Grad Center. A good interpersonal working environment is vital to any network based collaboration with deadlines, milestones, validation tests, release dates, and other organizational stresses. We will also sponsor bi-monthly retreat activities to relieve stress and to foster a unity of purpose. We will hold quarterly progress reviews, and in the second year, start a monthly business development meeting to focus on marketing our emerging technology and recruiting alpha test customers.

3.4.6.2 Project Management Software

Our company will use an open source development model. Open Source developers use SourceForge for network access to source code version management systems (code check-in, check out), mailing lists, bug tracking, message boards / forums, and task assignment, ownership, completion, and management. We will install the SourceForge project management software as private instance of the popular open source collaboration SourceForge.net web site. The principles behind SourceForge are use to hosts more than 12,000 open source projects.

We will support a DMT project at the CUNY Graduate Center on 34th St. and 5th, directly cross-town on is NYUMC. The CUNY Institute for Software Design and Development (CISDD) is a University Consortium that will act as the conduit for this project. The computer team is a short walk from the clinical facilities, which is crucial for fostering communication with our ultimate clients and customers.

3.4.6.3 Team members (TABLE)

Name		
Core Members	Affiliation	Role, Expertise and Task Areas

Professor D. B. Karron, PhD	CASI PI, CCNY	PI, DMT Inventor, C++, Computational Geometry, Computer Graphics, Algorithm Development, Will write DMT recoding core on server, market technology to prospective alpha customers and industries
Professor G Wolberg, PhD	CASI, CCNY	Lead Programmer. C++ programmer, algorithm development, digital image warping expert
Professor J L. Cox, PhD	CCNY	DMT developer, Theoretical computer scientist, analysis of algorithms.
Consulting Members		Encryption, Braid Theory, computational geometry, development
Professor M. Anshel, PhD	CCNY	of Braided DMT for Trajectory Planning and Analysis
Professor G. Herman, PhD	CCNY	Theory of surfaces, image segmentation, digital topology
Professor F. Bookstein, PhD	University of Michigan	Morphometrics, medical imaging and applied math
Mr. E. Gurfein, MBA	Meridian Resource and Development, Ltd.	VC fundraising for biotech, medical device, and chemistry startups; engineering venture capital, financial management and technical marketing
Clinical Participants	NYUMC Radiation Oncology	Breast cancer warrior using radiation therapy beams.
Chair S. Formenti, MD PhD		
Professor J. K. Dewyngaert, PhD	NYUMC Radiation Oncology	Radiation physicist; Specialist in prostate \cancer research using radiation and brachiotherapy
Professor and Col (Ret) R. A. Satava, MD	Yale University Medical Center Department of Surgery	Endoscopic and Virtual Reality in Medicine pioneer [illegible] DARPA - still works well.
Professor L. Liebis, PhD	NYU MC	Instrumentation specialist. Statistical epidemiology.
Chair R. Bucholz MD,	St. Louis University Medical Center, Department of Neurosurgery	Endoscopic surgeon and medical technology entrepreneur [illegible] Neurosurgeon and steriotactic neurosurgery system inventor [illegible] Potential alpha site [illegible]
S. V. Grasso, MD,	Stevens Institute of Technology and TIMA	Technology for Medical Integration (TIMA), robotic surgery expert and promoter
Post Doc/ Visiting Scientist		C++ image programming registration and warping, 3D modeling,
J. Patrichare, PhD (expected 2002)	Graduating from Mayo Clinic Medical Imaging PhD Program	
PhD graduate students	CUNY Graduate Center	Java programmer, System administrator, Web site designer and user interface tester
To be named; 3 total		

3.5 Potential for Broad-Based Economic Benefits

The nation will benefit by improved health care that will prolong the quality of life. Reduced employee sick leave will decrease disability related payouts and reduce costs to insurers. The efficient use of medical information will produce better yield on capital in imaging technology. Better patient and physician communication, treatment results, and patient satisfaction will result in less litigation and insurance costs. CASI will create new markets for model-based information as the core competency is established that will go beyond our initial Radiation Treatment project. As the medical imaging industry matures into the medical modeling industry, CASI will seek new markets for services, only dreamed of at present.

High technology medicine is widely viewed as beneficial the public, mainly because of the probability that any one of us may unexpectedly become the beneficiary of a new life saving therapies; However the costs of such technology to insurers, taxpayers, and the underinsured can be staggering. Expensive new hardware and drug offerings bombard the medical market. In a life-threatening situation, these high costs are relegated to a lower priority. When the bills have to be paid, and policymakers review galloping high technology medicine costs, they must consider the value to our society of "big iron" capital-intensive purchases such as multimillion-dollar diagnostic imaging facilities and therapeutic equipment. The value added to our nations' economy is that CASI will be a filter and conduit to increase the worth of this investment, by increasing the ability of medical diagnostic imaging to accomplish its promise: Save lives and keep us healthy.

3.5.1 National Economic Benefits

America is underutilizing the product of its diagnostic imaging capital base. The medical imaging industry is not making the best use of the mega pixels of patient data these systems generate. From an

information theoretic perspective, we estimate that 99% of that information is not contributing to the making of therapeutic decisions. We are not disseminating this information to all concerned parties rapidly and effectively. This is partly because we do not understand, use, or effectively model the important features in these images. This is because of limitations in the state of the art for understanding modeling key features, and applying this information in rapid and effective ways for broad base of radiologists, physicians, surgeons, and therapists. Further, we need to make it understandable to the ultimate customer, the patient, and / or the patients' family. New picture archiving and network distribution systems are helping to manage the raw data, the Next Generation Internet can make more of the raw data move faster, but the nation needs better technology to understand these images, make consistent precise patient specific determinations, and maximize the effective use for this data as essential insight. CASI will decrease the entropy and increase the pragmatic value of medical pixels by winnowing them down to geometric models, trajectory vectors, and critical points.

Customers include any radiologist, radiology practice, imaging facility, medical center, and associated diagnostic or therapeutic practitioner. The patient needs to be kept in the loop as the ultimate paying customer, and consumer of the therapeutic decisions based on this information. The customers that will benefit the most are any interpretative method of CT, MRI, PET, SPECT, etc. that currently is hand contouring stacks of images prefatory to designing a patient treatment, are evaluating the ongoing results of treatment. Similarly, anyone attempting to spot critical surgical targets, such as in steriotactic brain surgery, by sighting by the center of blobby objects in hundreds of slices will be a customer. Radiation Therapy (RT) practitioners were most eager to find better methods to eliminate this time consuming drudgery in their practice.

Competitors are scattered across various application area, using mainly volume rendering technology instead of shell surface technology. Most imaging companies are focused on one technology, almost to the exclusion of other application areas. Typically, these firms arise from image consulting firms working with one large customer with a specific application in petrology, histology, computer graphics, and so on. There are general-purpose visualization systems sponsored by government research labs (NCAR), and commercialization of large university programs (ANALYZE from Rich Robb's group at the Mayo Clinic), 3DVIEWNIX (From Jay Udupa's group at U. Penn). Commercial packages include Voxel View, AVS (Advanced Visualization System), Resolution3D, Khoros, IBM Data Explorer (DX), Iris Explorer, VTK tool kit (From Kitware) are but a few of the more popular general packages. Some have exceptional interactivity based on their optimization to special graphics accelerator hardware, now common with the explosion of the computer game industry). Many have intricate and comprehensive facilities for hand segmentation, contouring, snake segmentation, thresholding, flood filling, edge detection, marching cubes, and so on. None have anything that approaches the power and insight that Digital Morse Theory based segmentation can do to simplify many segmentation tasks. We will never manage to penetrate such a broad spread of markets, but we expect that we will license our technology and that will become an important source of revenue and diffusion of our technology and theory into the industry and broader national economy in ways we can barely foresee

End users are generally serviced by consultant using any of the above visualization packages. We will focus initially on the niche markets of Radiation Therapy and Neurosurgery as vehicles to develop our core technology. However, most of direct users will be software developers integrating our technology in their software packages for use by their individual specialty markets.

It is our plan to license our technology to other industries that can apply our technology are industrial non-destructive testing (industrial CT), meteorology, metrology, histopathology imaging, entertainment industry animation, medical illustration, commercial computer graphics for advertising, virtual reality, air traffic control, multimedia, medical education and training, simulation, topography, mapping, surveying, (not topology) fluid mechanics and dynamics modeling and visualization, hyperspectral scanner imaging, Earth Imaging Systems (for interpreting satellite imagery)

The benefits to the public are longer life, better quality of life, through improved medical care, at reduced cost through more effective delivery and utilization if medical imagery.

3.5.1.1 Business opportunities addressed and economic importance to proposer and the nation

Our business opportunity is the expense and time required to produce imprecise and inaccurate segmentations from which 3D models are generated for many disparate applications. There is no underlying paradigm for understanding how segmentation works. Most of the thinking current segmentation theory is *ad-hoc*, problem, and image specific, not repeatable, and requires an expert user. Discussions with robotic surgery designers and manufactures point out the problem designing robotic trajectories are bottlenecked with the patient specific modeling. Our core technology is being hailed as a breakthrough, if we can develop working systems from our concept demonstration. Alpha site customers and business interest is building as word of our possible technology circulates in our target markets. NYUMC Radiation and Oncology and St. Louis University have agreed to participate in our development effort as alpha test sites.

The economic important to CASI of this technology is based getting meaningful assistance in surgery from computer imaging. This requires 3D modeling on a rapid patient specific basis with precision, accuracy, and dimensional fidelity. This technology gap prompted the PI's research in this area and prompted our request for funding to develop this technology.

The economic importance to the nation is improving the utility and distribution of medical imaging information, and will improve the value of this expensive technology with our inexpensive, but Internet pervasive technology. Further, this is not a comparatively expensive technology in its application because we will use centralized computer servers, connected eventually, but not necessarily by Next Generation Internet or Internet II. Our value added is our intellectual property that will lead to improve health and longer life of American citizens.

3.5.1.2 Discussion of potential users of this technology

Patient specific anatomic modeling from medical imaging and true three-dimensional modeling is required by many medical specialties. The specialization of the physician based research groups and the lack of a common language and communication leads fractionation of effort. The results of style of research effort tends to degenerate the state of the art into a large collection of tricks, techniques, conflicting algorithms, and overloaded toolboxes. Most of these techniques lack an underlying mathematical rubric, uniform precision, and validation. Computer graphics has not provided the 'sound' solutions that it appears to illustrate. This is due to the lack of computational geometry and advanced math sophistication in the graphics industry. We see a wide range of medical, engineering, technical, and scientific users for our uniform approach and new technology.

CASI's DMT based technology has a number of potential users and applications. Our initial target markets are breast Radiation Therapy and neurosurgical steriotactic surgery. Once our technology has been show to be advantageous, it is expected that other specialties will utilize it. We will cultivate bellwether client collaborations in each surgical specialty, and market through their training programs with their residents and fellows, post doctoral students and visiting scientists. Expected application areas include: Cosmetic plastic surgery (modeling skin profile changes to sell cases to patients), Craniofacial surgery (model bone cuts, skin reconstruction due to trauma, birth defects, and cancer), Obstetrics (pelvis measurements are key parts of the decision to perform a caesarian), Oral surgery (tooth implants), Orthodontics (bone growth and effect of braces, selling cases to parents), Histopathology (cancer detection, cell type recognition, and cell counting), Biological shape analysis for surgical application.

3.5.1.2.1 Market estimates

At the end of this proposal, this technology will be successful for RT and Neurosurgery. At that time, for a cost of one hundred dollars the attending physician will a model of a patient's tumor, and be able to plan and demonstrate that plan for surgery or radiation.

In the RT focus area of our project, we measure the total market from cancer epidemiology. Unfortunately, we can expect an increased cancer rate in the future caused by environmental pollution. The survival rate due to better treatment technology will also increase. This increases the CASI market by an estimated 20%. CASI technology will be a part of that survival improvement.

Breast Cancer, the target of our RT collaboration at NYUMC saw ~176,300 new cases and 43,700 deaths in 1999. Prostate cancer had ~136 new cases per 100, 000 men. Surgical treatment brachiotherapy (treatment by implanting highly radioactive seed in the cancer) and RT are all require modeling and

targeting technology that is CASI's core technology.

Expected growth of markets opportunity by increased cases and increased survival of 20 % is assumed as CASI technology is embraced by medicine. Assuming a 20% market capture share, that means that in breast RT we can expect by the time of product roll out in 4 years to 42,000 cases / year. We can estimate a similar participation in prostate cancer therapy at 50,000 cases / year.

3.5.1.2.2 Markets change and new markets from new technology.

Our initial focus area is breast RT and Brain surgery. As we penetrate in these markets CASI will license its technology into other market areas; because we will need to focus the R & D effort on the generalized problem, and a few limited specific problem areas at a time. CASI will effectively franchise its technology into market application areas for maximal rapid diffusion. We estimate that we will be doing well over 10x our base RT revenue by franchising. CASI will promote bellwether researchers to adopt our technology for their specific application area by doing custom web interfaces to their spec, as CASI are developing our generalized application area.

3.5.2 Need for ATP funding

ATP funding is required to enable CASI to complete our ongoing research and make the technological leap to market of low cost, network based anatomic computer 'foundry' modeling. We will build on the progress we started making as a subcontractor on the NIH Visible Human Project (VHP) female 'Eve' dataset. The primary mission of the VHP program is to supply anatomic content for medical school education. CASI's broader therapeutic vision requires ATP development funding because the NIH mission in this area at this time is limited.

Segmentation and Registration issues impede progress in many disparate medical and scientific fields. No one industry or medical superspeciality has the patience to fund this development effort in the general case. Few programs share the vision of this technology for its broad applicability to medicine, technology, and science.

The visualization and modeling technology is not being effectively developed in the United States. The medical imaging industry is dominated by foreign owned and controlled companies such as Sony, Picker, Hitachi, Siemens, and General Electric. We believe that the market for pixel intensive hardware-accelerated graphics is wedged in the Internet last mile bottleneck. Wide diffusion for image-based information will require new thinking, not just more bandwidth. CASI will move from a "pixel based high entropy high bandwidth" representation to a "DMT based object geometry "representation with low entropy and high information theoretic pragmatic value.

3.5.2.1 Summary of efforts to get external and private funding

The CASI vision is to provide patient specific precise and accurate Level of Detail (LOD) models for diagnostic and therapeutic applications. CASI's raw input is medical images uploaded over the Internet. The time for development of this technology is too long for Venture Capitalist window of opportunity. We do not intend to become a medical computer graphics-imaging house, medical informatics consulting firm, or a surgical robotics firm. Our goal is to focus on solving the problems that are hindering the start of the art in radiation therapy, surgical robotics, 3D modeling, animation, and many other application areas. CASI's solution will become our core competency. The PI intends to aggressively grow the company into this wide-open opportunity field. CASI's broad therapeutic vision frightens private venture capitalists, and their funding. CASI is currently funded by angel investors and the PI. CASI will leap into the modeling business with ATP funding, and be able to focus on the long-term benefits of this technology.

CASI believes that it become profitable within 5 years, which is longer than the private equity market will tolerate. As we demonstrate our core technology by the third year, we expect that we will be able to rise significant private funding, but not before.

3.5.2.2 Description of how the technology will be broadly diffused

Broad diffusion of our technology will occur because of the strong need in a broad variety of medical and general scientific modeling applications. This strong gradient will pull our technology out of our lab and into commercial franchise or licensure-based adoption. Because the application runs as an ASP, anyone who can upload an image file will be able to run their image for a demonstration of the modeling facility, and see how the CASI system will solve their problems. The short time constant of internet based

technology diffuses out into the global community, and the strong needs gradient, means we can expect explosive growth in demand as we start public demonstrations and reporting our results in the literature and major scientific and medical meetings. CASI is preparing for this onslaught and will carefully not oversell its solutions and permit it to grow in managed and healthy manor for maximal benefit to the nation and for the company.

3.5.2.3 Business experience of PI and Staff

CASI was founded in 1995, while the PI was research professor of surgery at NYUMC. The PI has managed approximately one million dollars in DARPA funding, as well as such administrative tasks as running a payroll, subcontracting, DoD audits, Federal and State audits, bank audits, invoicing, collections, financing, and accounts payables with and without an administrative staff. CASI has kept meticulous records and attained a high professional standard under difficult business conditions. The PI has demonstrated fiscal responsibility managing significant federal funds responsibly. The PI has extensive technical management experience. Mr. E. Gurfein will be joining our team as our business manager, bringing his experience in scientific startup funding, finance, management, and marketing.

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